IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

CURRY et al. Examiner: R. Anderson

Serial No.: 09/673,473 Art Unit: 1626

Filed: November 29, 2000

For: **CUBANE DERIVATIVES AS METABOTROPIC GLUTAMATE RECEPTOR AGONISTS OR ANTAGONISTS AND PROCESS FOR THEIR PREPARATION**

Appendix B

Please amend the following claim as indicated in the following clean copy of the claims.

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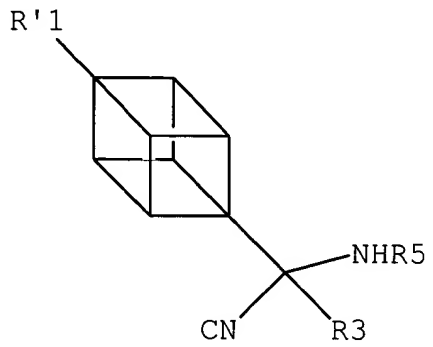
5. (Twice Amended) A process for the preparation of a compound of Formula I as claimed in claim 1, or a pharmaceutically acceptable metabolically-labile ester or amide thereof, or a pharmaceutically acceptable salt thereof, which comprises:

(a) hydrolyzing a compound of formula:



(II)

wherein: **R'1** is an acidic group selected from the group consisting of carboxyl, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, -CH_2-carboxyl, -CH_2-phosphono, -CH_2-phosphino, -CH_2-sulfono, -CH_2-sulfino, -CH_2-borono, -CH_2-tetrazol, -CH_2-isoxazol and higher analogues thereof, or a protected form thereof, **R3** can be H, aliphatic, aromatic or heterocyclic and **R5** represents a hydrogen atom or an acyl group, and wherein preferred values for **R5** are hydrogen and (2-6C) alkanoyl groups, such as acetyl; or

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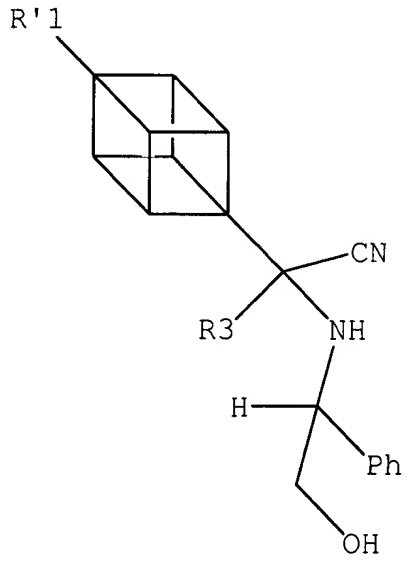
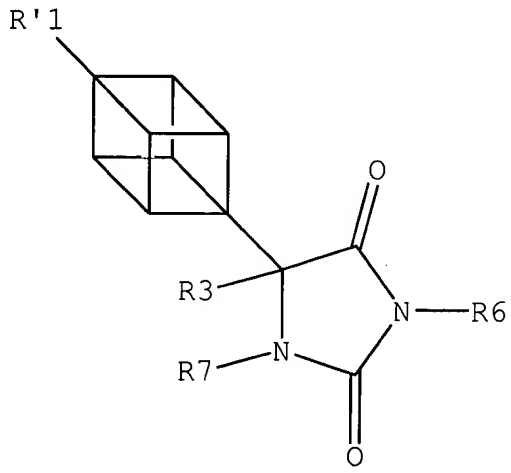
(b) deprotecting and hydrolyzing a compound of formula (IIb):



(IIb)

wherein: **R'1** and **R3** are as defined above; or

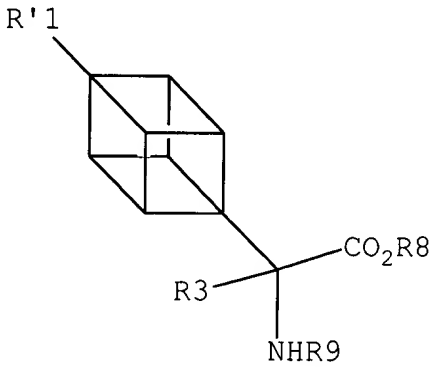
(c) hydrolyzing a compound of formula:



(III)

wherein: **R6** and **R7** each independently represent a hydrogen atom, a (2-6C) alkanoyl group, a (1-4C) alkyl group, a (3-4C) alkenyl group or a phenyl (1-4C) alkyl group in which the phenyl is unsubstituted or substituted by halogen, (1-4C) alkyl or (1-4C) alkoxy, or a salt thereof, **R'1** and **R3** are as defined above; or

(d) deprotecting a compound of formula:



(IV)

wherein: **R8** represents a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R9** represents a hydrogen atom or a nitrogen protecting group, **R'1** and **R3** are as defined above;

whereafter, if necessary and/or desired:

(i) resolving the compound of Formula I;

(ii) converting the compound of Formula I into a non-toxic metabolically-labile ester or amide thereof; and/or

(iii) converting the compound of Formula I or a non-toxic metabolically-labile ester or amide thereof into a pharmaceutically acceptable salt thereof.

B2

7. (Twice Amended) A method of modulating one or more metabotropic glutamate receptor functions in a warm blooded mammal, comprising administering an effective amount of a compound of formula (I) as claimed in claim 1 to a warm blooded mammal in need thereof.

B3

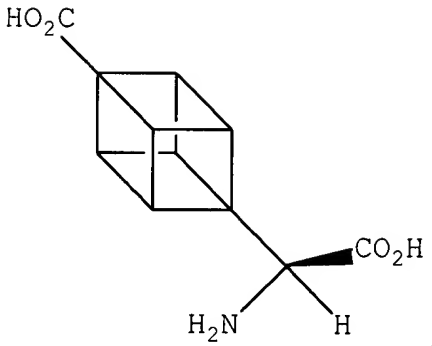
14. (Once Amended) A method of treating a neurological disease or disorder in a warm blooded mammal comprising administering an effective amount of the compound of formula (I) according to claim 1 to a warm blooded mammal in need thereof, wherein said neurological disease or disorder is selected from the group consisting of cerebral deficits subsequent to cardiac bypass surgery and grafting, cerebral ischemia, stroke, cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, and hypoglycemic neuronal damage, Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia,

ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance, withdrawal, and cessation (i.e. opiates, benzodiazepines, nicotine, cocaine, or ethanol), smoking cessation, anxiety and related disorders (e.g. panic attack), emesis, brain edema, chronic pain, sleep disorders, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia.

B3 Cont'd

15. (Once Amended) A method of treating a psychiatric disease or disorder in a warm blooded mammal comprising administering an effective amount of the compound of formula (I) according to claim 1 to a warm blooded mammal in need thereof, wherein said psychiatric disease or disorder is selected from the group consisting of schizophrenia, anxiety and related disorders (e.g. panic attack), depression, bipolar disorders, psychosis, and obsessive compulsive disorders.

16. (Once Amended) The method according to claim 7 wherein said compound is selected from the group consisting of



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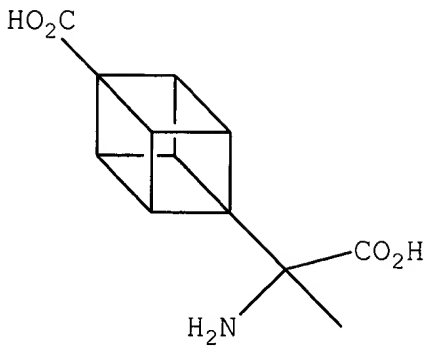

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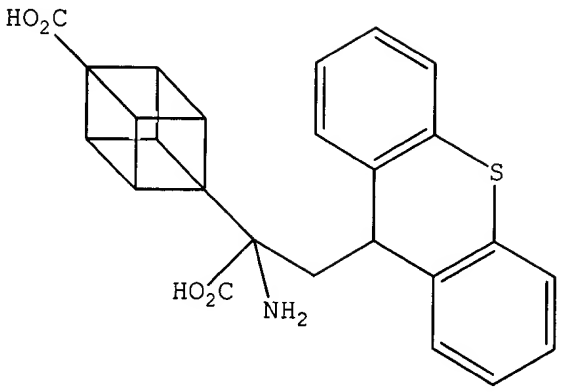

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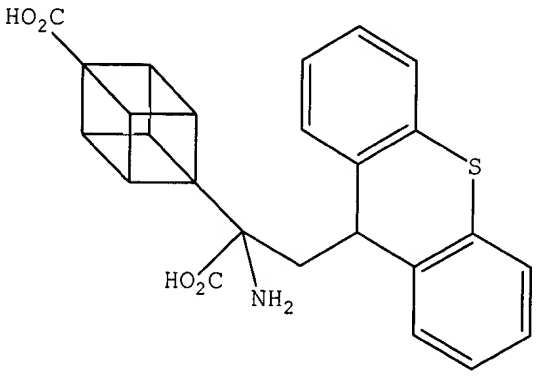
17. (Once Amended) A method of treating cerebral ischemia, stroke and cardiac arrest in a warm blooded mammal comprisingadministering an effective amount of the compound



to a warm blooded mammal in need thereof.